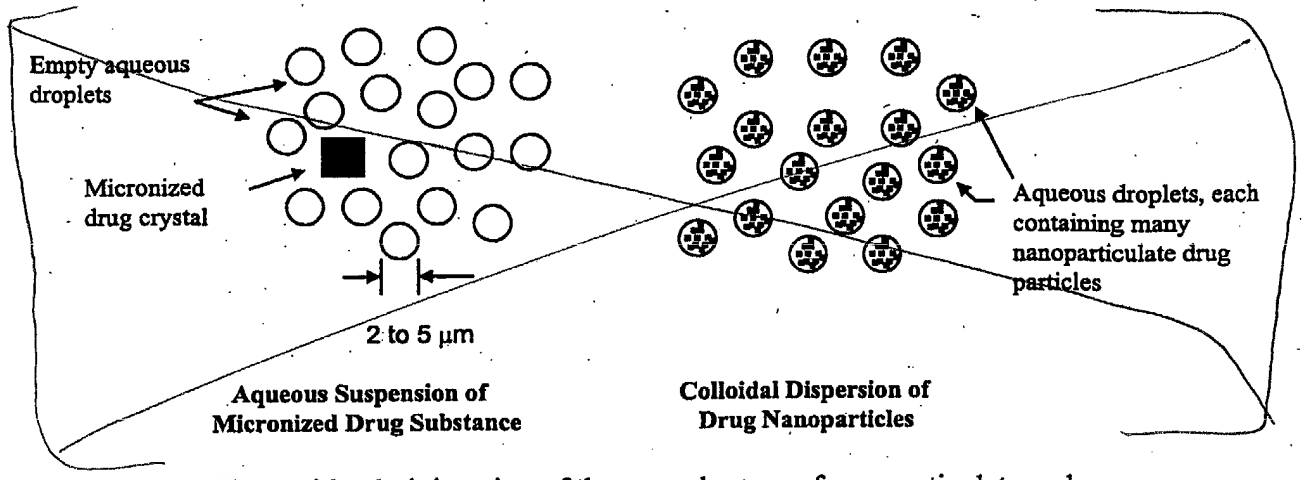
than the droplets in such an aerosol. Thus, aerosols containing nanoparticulate drug particles improve drug delivery efficiency because they contain a higher number of drug particles per unit dose such that each aerosolized droplet contains active drug substance.



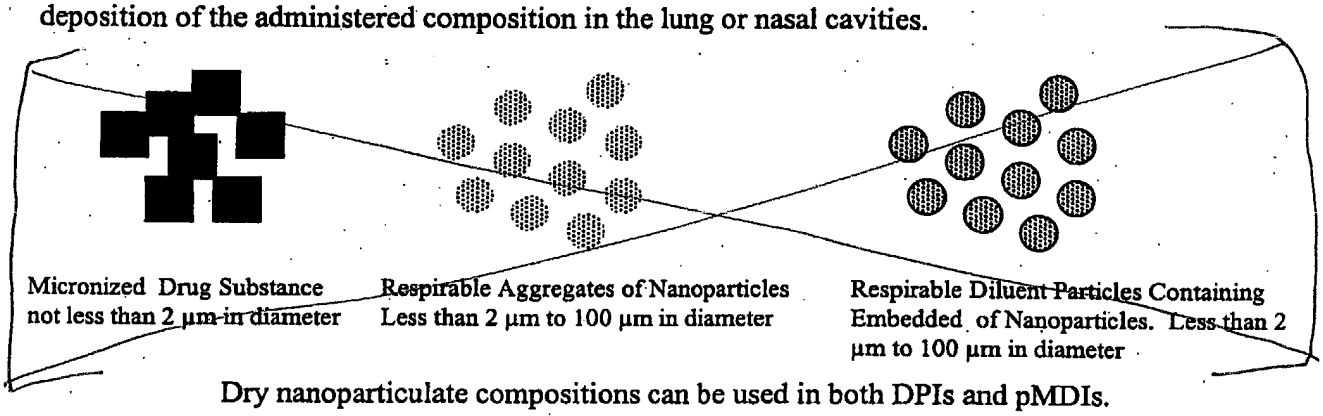
Thus, with administration of the same dosages of nanoparticulate and micronized drug, more lung or nasal cavity surface area is covered by the aerosol formulation containing nanoparticulate drug.

Another advantage of the present invention is that it permits water-insoluble drug compounds to be delivered to the deep lung via nebulization of aqueous formulations. Conventional micronized drug substance is too large to reach the peripheral lung regardless of the size of the droplet produced by the nebulizer, but the present invention permits nebulizers which generate very small (about 0.5 to about 2 microns) aqueous droplets to deliver water-insoluble drugs in the form of nanoparticles to the alveoli. One example of such devices is the Circulaire® (Westmed Corp., Tucson, AZ).

Yet another advantage of the present invention is that ultrasonic nebulizers can be used to deliver water-insoluble drugs to the lung. Unlike conventional micronized material, nanoparticulate drug particles are readily aerosolized and show good *in vitro* deposition characteristics. A specific advantage of the present invention is that it permits water-insoluble drugs to be aerosolized by ultrasonic nebulizers which require the drug substance to pass through very fine orifices to control the size of the aerosolized droplets. While conventional drug material would be expected to occlude the pores, nanoparticulate drug particles are much smaller and can pass through the pores without difficulty.

which actually reaches the alveolar region may be quite small. Thus, delivery of micronized dry powders to the lung, especially the alveolar region, is generally very inefficient because of the properties of the powders themselves.

The dry powder aerosols which contain nanoparticulate drugs can be made smaller than comparable micronized drug substance and, therefore, are appropriate for efficient delivery to the deep lung. Moreover, aggregates of nanoparticulate drugs are spherical in geometry and have good flow properties, thereby aiding in dose metering and deposition of the administered composition in the lung or nasal cavities.



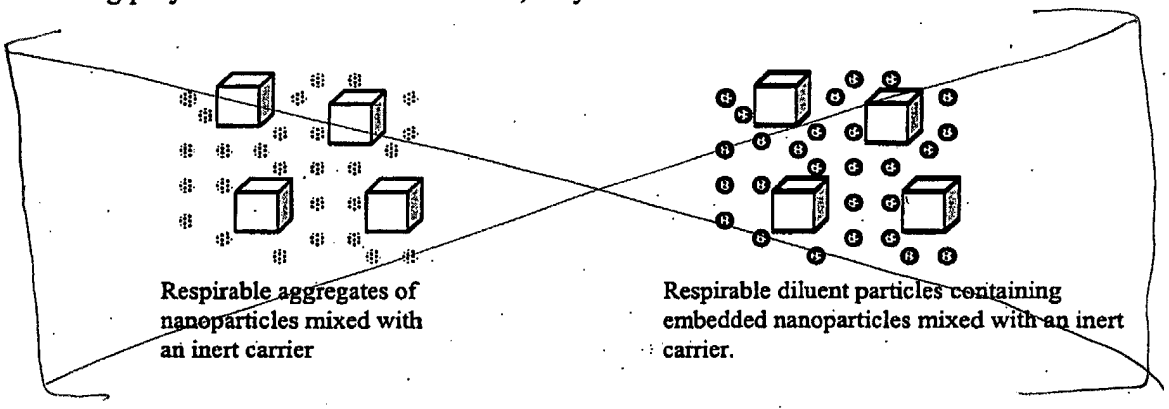
Dry nanoparticulate compositions can be used in both DPIs and pMDIs. (In this invention, "dry" refers to a composition having less than about 5% water.)

6. Propellant-Based Aerosols

Another embodiment of the invention is directed to a process and composition for propellant-based MDIs containing nanoparticulate drug particles. pMDIs can comprise either discrete nanoparticles of drug and surface modifier, aggregates of nanoparticles of drug and surface modifier, or inactive diluent particles containing embedded nanoparticles. pMDIs can be used for targeting the nasal cavity, the conducting airways of the lung, or the alveoli. Compared to conventional formulations, the present invention affords increased delivery to the deep lung regions because the inhaled nanoparticulate drug particles are smaller than conventional micronized material (< 2 µm) and are distributed over a larger mucosal or alveolar surface area as compared to micronized drugs.

nozzle. For deep lung delivery it is desirable for the collected product size to be less than about 2 μm in diameter; for delivery to the conducting airways it is desirable for the collected product size to be about 2 to about 6 μm in diameter, and for nasal delivery a collected product size of about 5 to about 100 μm is preferred. Collected products may then be used in conventional DPIs for pulmonary or nasal delivery, dispersed in propellants for use in pMDIs, or the particles may be reconstituted in water for use in nebulizers.

In some instances it may be desirable to add an inert carrier to the spray-dried material to improve the metering properties of the final product. This may especially be the case when the spray dried powder is very small (less than about 5 μm) or when the intended dose is extremely small, whereby dose metering becomes difficult. In general, such carrier particles (also known as bulking agents) are too large to be delivered to the lung and simply impact the mouth and throat and are swallowed. Such carriers typically consist of sugars such as lactose, mannitol, or trehalose. Other inert materials, including polysaccharides and cellulosics, may also be useful as carriers.



Spray-dried powders containing nanoparticulate drug particles may used in conventional DPIs, dispersed in propellants for use in pMDIs, or reconstituted in a liquid medium for use with nebulizers.